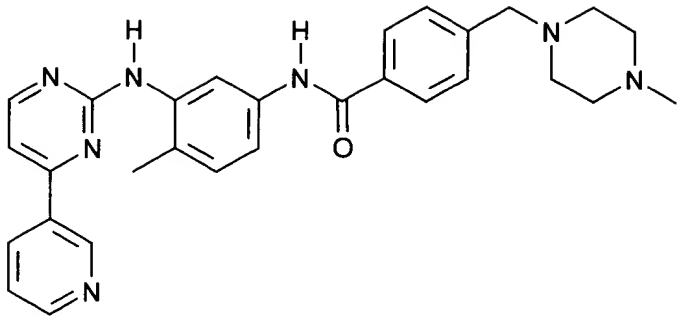


in its β-crystal modification.

STATUS OF THE CLAIMS

Claims 1-8, 10 and 12-16 will be pending in this application upon entry of this amendment.

Claims 1-8 and 15-16 are rejected under 35 USC 112, second paragraph.

Claims 1-8, 10, 13-15 are rejected under 35 USC 102(b) and 35 USC 103(a) over Zimmermann.

Claim 12 is rejected under 35 USC 103(a) over Zimmermann in view of Yu.

Claims 1-8, 10 and 12-16 are presented for reconsideration.

REMARKS

Applicants confirm that it was intended to cancel claim 11, and not claim 10, in the previous Amendment. Applicants appreciate the Examiner's attention to this matter. Based on the Office action, Applicants understand that claim 10 is now pending, and claim 11 is now cancelled.

Claims 1-8 and 15-16 are rejected under 35 USC 112, second paragraph. Applicants request reconsideration and withdrawal of this rejection for the reasons that follow.

The Examiner asserts that claims 4-8, 1 and 6, and 15 and 16 do not materially differ from one another. Applicants direct the Examiner to MPEP 706.03(k) which indicates that court decisions have confirmed applicant's right to restate (i.e. by plural claiming) the invention in a reasonable number of ways. A mere difference in scope has been held to be enough. Applicants

assert that each of claims 4-8 is of a different scope from the others; claims 4 and 5 by the different melting points recited in the claims and claims 6-8 by the different specificity of the x-ray diffraction requirements of the crystal form. Likewise, claims 1 and 6 are of different scope from each other because claim 6 requires the crystalline form to show a specific x-ray diffraction characteristic in addition to being non-hydroscopic and crystalline, and claims 15 and 16 define the x-ray diffraction characteristics with a different degree of specificity. Applicants assert that the metes and bounds of the claims discussed above are definite to one of skill in the art and that the rejection under 35 USC 112, second paragraph, should be withdrawn.

With regard to process claim 12, the Examiner questions how the same or overlapping reaction conditions can achieve simultaneously dissolution and digestion. Applicants point out that parts (a) and (b) of claim 12 are alternatives. Therefore, the claim does not require simultaneous dissolution and digestion. In addition, claim 12 is not limited to any particular solvents. The first paragraph on page 7 of the specification teaches certain solvents that are useful to prepare the crystalline form by digesting another crystal form under the conditions specified in part (a) of claim 12 and other solvents that are useful to prepare the crystalline form by dissolving another crystal form and recrystallizing under the conditions specified in part (b) of claim 12. Thus, claim 12 claims two different alternative processes for making the subject crystalline form. Preparing the subject crystalline form by either of these alternative processes infringes claim 12. Thus, Applicants assert that the metes and bounds of claim 12 are definite to one of skill in the art and that the rejection under 35 USC 112, second paragraph, should be withdrawn. Applicants also would agree to convert claim 12 into two independent claims if the Examiner would prefer.

Applicants believe that all rejections under 35 USC 112, second paragraph, are addressed above. Therefore, withdrawal of all rejections under 35 USC 112, second paragraph, is requested for the reasons discussed above.

Claim 14 was rejected under 35 USC 112, first paragraph. The claim has been amended so that it no longer claims the treatment of any and all tumor types. Applicants assert that the disclosure provides adequate support and enablement for the types of cancer and tumors treated by the claimed method. See, for example, pages 10 and 11 of the disclosure. Therefore, Applicants request withdrawal of the rejection of claim 14 under 35 USC 112, first paragraph.

Claims 1-8, 10, 13-15 are rejected under 35 USC 102(b) and 35 USC 103(a) over Zimmermann, and claim 12 is rejected under 35 USC 103(a) over Zimmermann in view of Yu. Applicants request reconsideration and withdrawal of these rejections for the reasons that follow.

Applicants note that claim 16 was not included in either rejection and request clarification of whether the Examiner intended to include it.

The mesylate salt of 4-(4-methylpiperazin-1-ylmethyl)-N-{4-methyl-3-(pyridin-3-yl)pyrimidin-2-ylamino)phenyl]benzamide (represented by the structure of claim 1) has been approved by the FDA and has been given the generic name imatinib mesylate. It is marketed in the U.S. under the Gleevec™ brand. For the sake of simplicity, the generic name will be used in the following discussion.

The present claims are limited to a specific crystalline form of imatinib mesylate, and do not claim imatinib mesylate *per se*. Since the disclosure indicates that imatinib mesylate exists in at least two different crystalline forms, only one which is non-hydroscopic under the conditions set forth in the claims and/or shows the specified characteristics in the x-ray diffraction pattern, if issued, the present claims would not prevent a third party from making, using and selling what the Examiner asserts is anticipated by Zimmermann - the mesylate salt of the subject compound. Such claims only prevent the making, using and selling (etc.) of the claimed crystalline form. Clearly, there is a distinction between claims covering a mesylate salt of a compound and a particular crystalline form of that mesylate salt.

The Examiner appears to agree that while Zimmermann specifically discloses imatinib, the mesylate salt is not prepared in the reference. In order to reject the present claims, the Examiner asserts that Zimmermann discloses a narrow well defined class of compounds which includes the mesylate salt of imatinib (In re Petering) and that the mesylate salt of imatinib is inherently disclosed by Zimmermann (In re Best, In re Fitzgerald, In re Grose). The Examiner relies on this case law to contend that it is Applicants' burden to show that the claimed crystalline form cannot be made following routine conditions.

However, Applicants assert that the Examiner's position regarding Applicants' burden to overcome the anticipation rejection is not consistent with the holding in Glaxo v. Novopharm, 34 USPQ2d 1565 (Fed. Cir. 1995) ("Glaxo"). In Glaxo, a case with factual circumstances similar to the present facts, the Federal Circuit held that for the prior art to inherently anticipate a claim directed to

a crystalline form of a compound, the reference must contain disclosure that would invariably produce the claimed crystal form when followed by one of skill in the art.

The Glaxo case related to U.S. Patent No. 4,521,431 with claims to a crystal form of a drug substance, the crystal form of ranitidine hydrochloride designated Form 2. U.S. Patent No. 4,128,658, the prior art, specifically disclosed ranitidine hydrochloride and a process for preparing it in Example 32. The district court found that the evidence demonstrated that both the Form 1 and Form 2 crystal forms could be prepared by following the disclosure of Example 32 of the '658 patent. The District Court held and the Federal Circuit affirmed that the '658 patent did not inherently anticipate a patent claim directed to Form 2 ranitidine hydrochloride because one of skill in the art following Example 32 did not inevitably produce the Form 2 polymorph (i.e. because either Form 1 or Form 2 could be made). The fact that the skilled artisan **could** produce Form 2 ranitidine hydrochloride by following the teaching of the reference was not sufficient render invalid a composition of matter claim to Form 2 ranitidine hydrochloride. Thus, according to Glaxo, an inherent anticipation is proper only in circumstances where the claimed subject matter is inevitably produced by following the teaching of the reference.

In the present instance, Zimmermann does not disclose any specific procedure for preparing imatinib mesylate. It merely suggests that mesylate salts of the disclosed compounds could be prepared. Moreover, the Examiner has not even alleged that anything in the reference leads the skilled artisan to expect that imatinib mesylate would exist in more than one crystal form when it was actually made. Because the presently claimed crystalline form is not the inevitable result of following the teaching of Zimmermann and because nothing in Zimmermann suggests that imatinab mesylate would exist in more than one crystal form, Applicants assert, in accordance with the Glaxo decision, that Zimmermann does not render claims to a crystalline form of imatinib mesylate unpatentable under either of 35 USC 102 or 103.

In response to the Examiner's reliance on In re Best and In re Fitzgerald these cases are distinguishable from the present circumstances because both cases relate to instances where the patent applicant was unable to satisfactorily differentiate the claimed product from the product actually made in the prior art. In the present case, since imatinib mesylate was not actually made in the reference, there is no prior art form of imatinib mesylate from which the claimed crystalline form needs to be differentiated.

In re Grose is also based on the patent applicant's failure to present sufficient evidence to demonstrate that the claimed zeolite was different from a zeolite actually made in the prior art. See, page 63:

> "The present record does not support the conclusion that appellants' zeolite and Milton's zeolite R are zeolites having different crystal structures. The admitted permissible variations in the diffraction data of appellants' zeolite would embrace, at least prima facie, the diffraction data disclosed for Milton's zeoliteR. Thus, this is not a situation where the difference in diffraction pattern could only be attributed to a difference in crystal structure."

Applicants have previously distinguished the present facts from the In re Petering decision. Applicants' previous response is incorporated by reference. In response to the Examiner's assertions in the present Office action, Applicants again assert that nothing in Zimmermann teaches or suggests anything about the properties of the various salt forms of any of the disclosed compounds. More specifically, Applicants assert that Zimmermann makes no teaching that imitanib mesylate would exist in more than one crystal form or suggest anything about the properties of such crystal forms.

Applicants further assert that the Examiner's continued reliance on Petering is inconsistent with the Glaxo case cited above. Glaxo held that a crystal form of ranitidine hydrochloride was patentable over a different crystal form of the same compound. If the disclosure of the exact salt, ranitidine hydrochloride, did not anticipate other crystal forms of the same salt, Applicants do not understand how the Zimmermann reference can be properly relied upon as anticipating undisclosed crystal forms of a salt that is not even prepared in the reference.

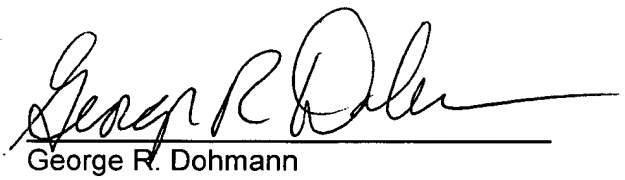
Applicants further point out that the Grose opinion is consistent with Glaxo because the CCPA clearly indicates that claimed zeolite would have been patentable if the patent applicant had satisfactorily demonstrated that the claimed zeolite had a different crystal structure from Milton's. See, 201 USPQ page 64 where the CCPA cites In re Cofer, 148 USPQ 268, 271 (CCPA 1966) to indicate that after finding the claimed zeolite different from the prior art, the board improperly rejected the claims for obviousness because an obviousness determination requires consideration of whether the prior art suggests the particular structure or form of the composition as well as methods for obtaining that structure or form. In the present case, the prior art does not suggest any particular form of imatinib mesylate or suggest that any particular form could be made by a particular method. Thus, the Grose opinion also supports Applicants' position that the inventive

crysalline form of imatinib mesylate is not anticipated by or obvious over the disclosure of Zimmermann.

For the reasons discussed above, Applicants request reconsideration and withdrawal of all rejections under 35 USC 102 and/or 103.

Entry of this amendment and reconsideration and allowance of the claims are earnestly solicited.

Respectfully submitted,



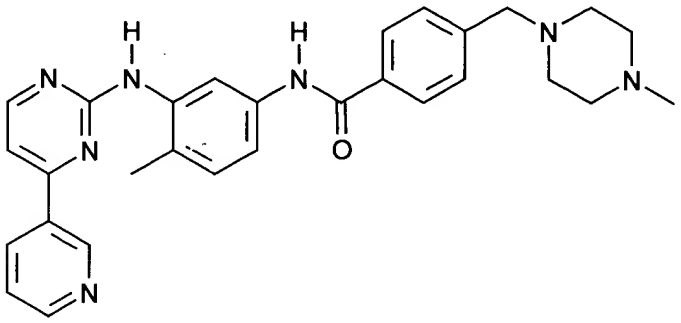
George R. Dohmann
Attorney for Applicants
Reg. No. 33,593

Novartis Corporation
Patent and Trademark Dept.
564 Morris Avenue
Summit, NJ 07901-1027
(908) 522-6922

Date: October 3, 2001

Appendix – Marked-Up Version of Amended Claim

14. (once amended) A method for treating a c-kit or BCR-abl positive cancer or tumor disease in a patient, which comprises administering to the patient an effective amount of a compound of the formula



in its β-crystal modification.